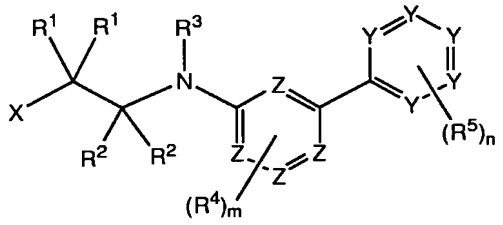
What is claimed is:

1. A compound for modulating kinase activity, particularly Tie-2, of Formula **I**,



I

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

X is selected from -H, $-OR^6$, $-S(O)_{0-2}R^6$, $-N(R^6)R^7$, $-O-N(R^6)R^7$, $-N(R^6)OR^6$, $-N(R^6)N(R^6)R^7$, absent, oxo, thiono, and imino, with the proviso that when X is oxo, thiono, or imino, there is only one R^1;

R^1 and R^2, at each occurance, are each independently selected from -H, halogen, -CN, $-NH_2$, $-NO_2$, $-OR^6$, $-N(R^6)R^7$, $-S(O)_{0-2}R^7$, $-SO_2N(R^6)R^7$, $-CO_2R^6$, $-C(O)N(R^6)R^7$, $-N(R^6)SO_2R^7$, $-N(R^6)C(O)R^7$, $-N(R^6)CO_2R^7$, $-C(O)R^6$, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, absent, and optionally substituted lower heterocyclylalkyl;

optionally two of R^2 together are oxo;

optionally, at least one pair of substituents, selected from two of R^1, two of R^2, and one each of R^1 and R^2, together with the corresponding carbon or carbons to which they are attached, form a first ring comprising between three and seven annular atoms, said first ring optionally substituted with between zero and four additional of R^1, each independently selected as defined above and optionally, when paired, together with the corresponding atom or atoms of the first ring to which they are attached, form a second ring comprising between three and seven annular atoms, said second ring optionally substituted with between zero and three of R^1;

R^3 is selected from -H, optionally substituted lower alkyl, optionally substituted lower arylalkyl, optionally substituted aryl, optionally substituted heterocyclyl, and optionally substituted alkoxy;

optionally R^3 and one of R^2, together with the atoms to which each is attached, form a third ring comprising between three and seven annular atoms, said third ring optionally

substituted with between zero and four additional of R^1, each independently selected as defined above and optionally, when paired, together with the corresponding atom or atoms of the third ring to which they are attached, form a fourth ring comprising between three and seven annular atoms, said fourth ring optionally substituted with between zero and three of R^1;

optionally R^3 and one of R^1, together with the atoms to which they are attached and the carbon to which R^2 is attached, form a fifth ring comprising between three and seven annular atoms atoms, said fifth ring optionally substituted with between zero and four additional of R^1, each independently selected as defined above and optionally, when paired, together with the corresponding atom or atoms of the fifth ring to which they are attached, form a sixth ring comprising between three and seven annular atoms, said sixth ring optionally substituted with between zero and three of R^1;

m is zero to four;

each of R^4 is independently selected from -H, halogen, -CN, $-NH_2$, $-NO_2$, $-OR^6$, $-N(R^6)R^7$, $-S(O)_{0-2}R^7$, $-SO_2N(R^6)R^7$, $-CO_2R^6$, $-C(O)N(R^6)R^7$, $-N(R^6)SO_2R^7$, $-N(R^6)C(O)R^7$, $-N(R^6)CO_2R^7$, $-C(O)R^6$, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

optionally two adjacent of R^4, together with the two carbons to which they are attached, form a seventh ring fused with the aromatic ring system containing Z as in Formula **I**, said seventh ring comprising between five and seven atoms and substituted with zero to three additional of R^4, provided said seventh ring together with the aromatic ring system containing Z as in Formula **I** does not constitute a 7-deazapurine;

each Y is independently either $=C(R^5)-$ or =N-, provided that there are no more than three of =N- in the aromatic ring bearing Y;

each Z is independently either $=C(R^4)-$ or =N-;

n is zero to five;

each R^5 is independently selected from -H, halogen, -CN, $-NH_2$, $-NO_2$, $-OR^6$, $-NR^6R^7$, $-S(O)_{0-2}R^7$, $-SO_2NR^6R^7$, $-CO_2R^6$, $-C(O)NR^6R^7$, $-N(R^6)SO_2R^7$, $-N(R^6)C(O)R^7$, $-N(R^6)CO_2R^7$, $-C(O)R^6$, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

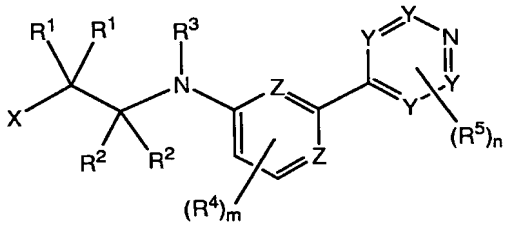
optionally two adjacent of R^5, together with the two carbons to which they are attached, form an eighth ring fused with the aromatic ring system containing Y as in Formula **I**, said eighth ring comprising between five and seven atoms and substituted with zero to three additional of R^5;

R^6 is -H or R^7;

R^7 is selected from optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

R^6 and R^7, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P.

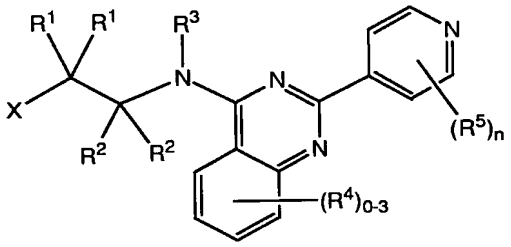
2. The compound according to claim 1, of Formula **II**.



II

3. The compound according to claim 2, wherein at least one of Z is =N-.

4. The compound according to claim 3, of Formula **III**.



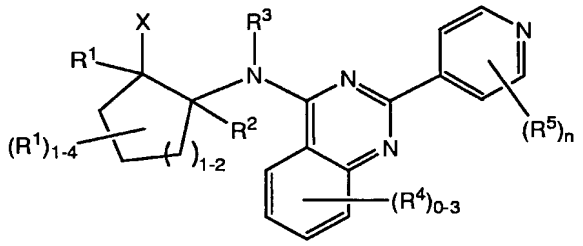
III

5. The compound according to claim 4, wherein one each of R^1 and R^2, together with the corresponding carbons to which they are attached, form said first ring, said first ring

comprising a saturated ring, said saturated ring optionally substituted with between zero and four additional of R^1.

6. The compound according to claim 5, wherein said saturated ring is carbocyclic.

7. The compound according to claim 6, of Formula **IV**.

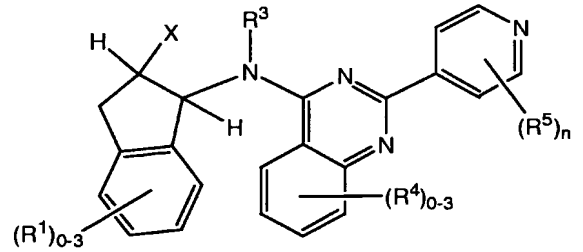


IV

8. The compound according to claim 7, wherein two of R^1, together with the carbon or carbons to which they are attached, form said second ring.

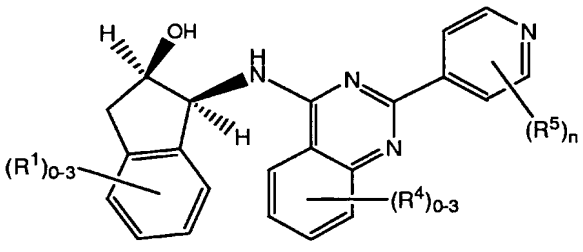
9. The compound according to claim 8, wherein said second ring is a six-membered aryl, fused with said first ring, said second ring optionally substituted with between zero and three of R^1.

10. The compound according to claim 9, of formula **V**.



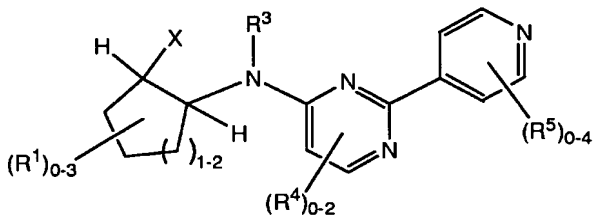
V

11. The compound according to claim 10, of formula **VI**.



VI

12. The compound according to claim 3, of formula **VII**,

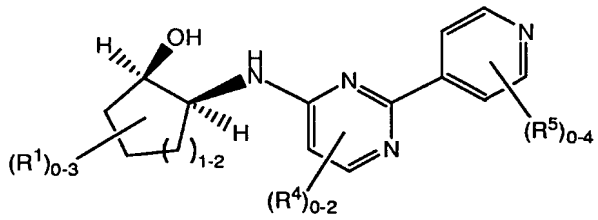


VII

13. The compound according to claim 12, wherein at least one of R^1 is an optionally substituted aryl or an optionally substituted phenyl.

14. The compound according to claim 12, wherein at least one of R^4 is an optionally substituted aryl or an optionally substituted phenyl.

15. The compound according to claim 12, of formula **VIII**.



VIII

16. The compound according to claim 15, wherein two of R^4, together with the aromatic annular atoms to which they are attached, form said seventh ring, said seventh ring comprising between zero and two nitrogens.

17. The compound according to claim 16, wherein said seventh ring is substituted with between zero and three additional of R^4.

18. The compound according to claim 1, selected from Table 3.

Table 3

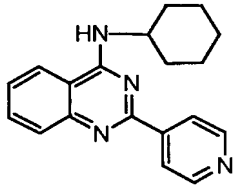
#	Name	Structure
1	N-cyclohexyl-2-pyridin-4-ylquinazolin-4-amine	

Table 3

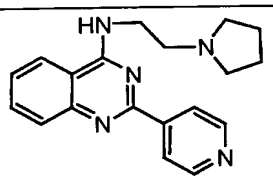
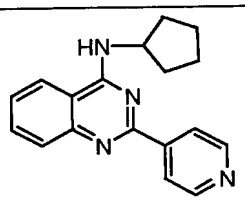
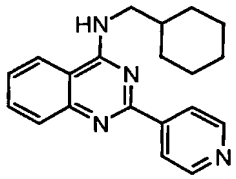
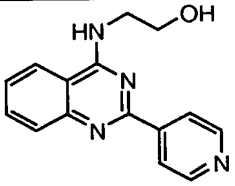
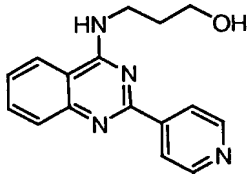
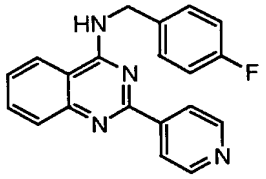
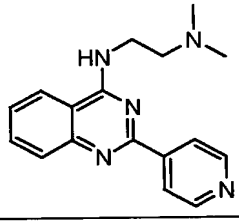
#	Name	Structure
2	2-pyridin-4-yl-N-(2-pyrrolidin-1-ylethyl)quinazolin-4-amine	
3	N-cyclopentyl-2-pyridin-4-ylquinazolin-4-amine	
4	N-(cyclohexylmethyl)-2-pyridin-4-ylquinazolin-4-amine	
5	2-[(2-pyridin-4-ylquinazolin-4-yl)amino]ethanol	
6	3-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-1-ol	
7	N-[(4-fluorophenyl)methyl]-2-pyridin-4-ylquinazolin-4-amine	
8	N,N-dimethyl-N'-(2-pyridin-4-ylquinazolin-4-yl)ethane-1,2-diamine	

Table 3

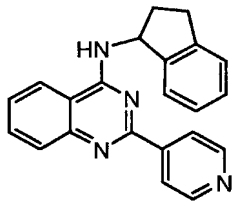
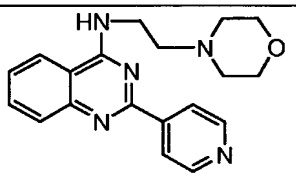
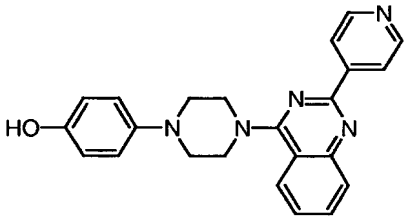
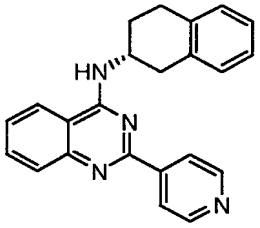
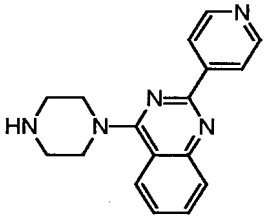
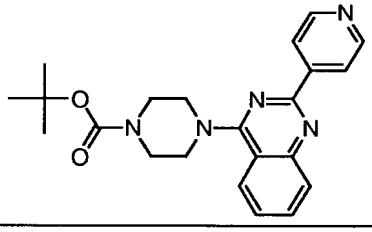
#	Name	Structure
9	N-(2,3-dihydro-1H-inden-1-yl)-2-pyridin-4-ylquinazolin-4-amine	
10	N-(2-morpholin-4-ylethyl)-2-pyridin-4-ylquinazolin-4-amine	
11	4-[4-(2-pyridin-4-ylquinazolin-4-yl)piperazin-1-yl]phenol	
12	2-pyridin-4-yl-N-[(2R)-1,2,3,4-tetrahydronaphthalen-2-yl]quinazolin-4-amine	
13	4-piperazin-1-yl-2-pyridin-4-ylquinazoline	
14	1,1-dimethylethyl 4-(2-pyridin-4-ylquinazolin-4-yl)piperazine-1-carboxylate	

Table 3

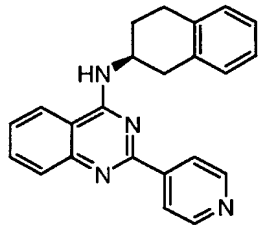
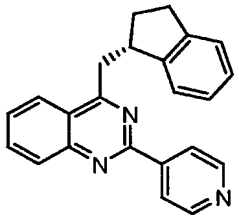
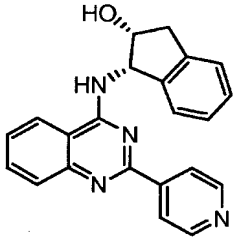
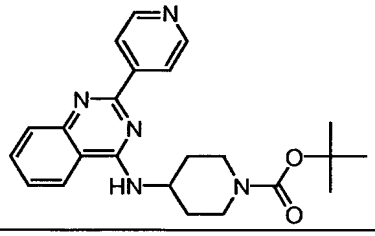
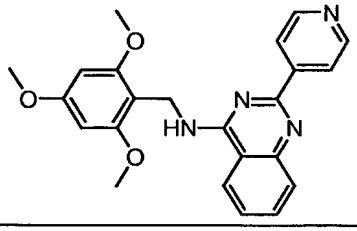
#	Name	Structure
15	2-pyridin-4-yl-N-[(2S)-1,2,3,4-tetrahydronaphthalen-2-yl]quinazolin-4-amine	
16	4-[(1S)-2,3-dihydro-1H-inden-1-ylmethyl]-2-pyridin-4-ylquinazoline	
17	(1R,2S)-1-[(2-pyridin-4-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
18	(1S,2R)-1-[(2-pyridin-4-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
19	1,1-dimethylethyl 4-[(2-pyridin-4-ylquinazolin-4-yl)amino]piperidine-1-carboxylate	
20	2-pyridin-4-yl-N-{[2,4,6-tris(methyloxy)phenyl]methyl}quinazolin-4-amine	

Table 3

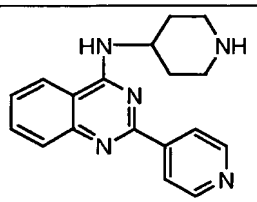
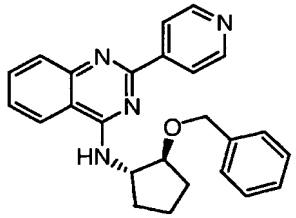
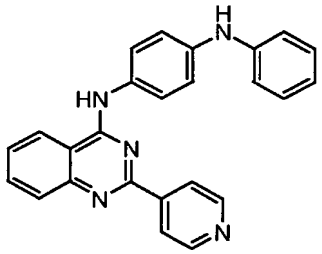
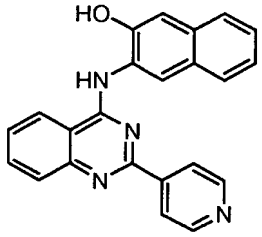
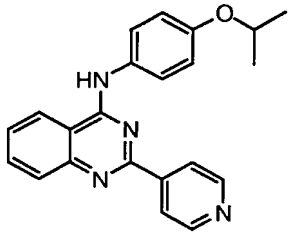
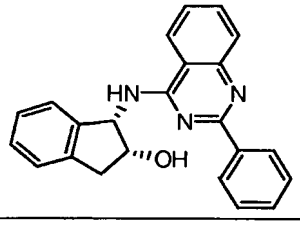
#	Name	Structure
21	N-piperidin-4-yl-2-pyridin-4-ylquinazolin-4-amine	
22	N-{(1S,2S)-2-[(phenylmethyl)oxy]cyclopentyl}-2-pyridin-4-ylquinazolin-4-amine	
23	N-phenyl-N'-(2-pyridin-4-ylquinazolin-4-yl)benzene-1,4-diamine	
24	3-[(2-pyridin-4-ylquinazolin-4-yl)amino]naphthalen-2-ol	
25	N-{4-[(1-methylethyl)oxy]phenyl}-2-pyridin-4-ylquinazolin-4-amine	
26	(1S,2R)-1-[(2-phenylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	

Table 3

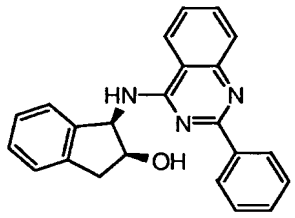
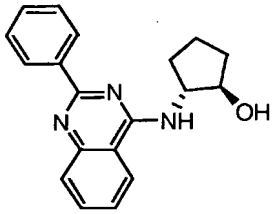
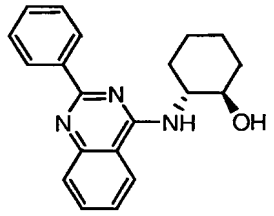
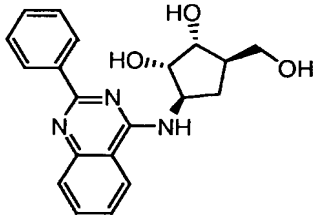
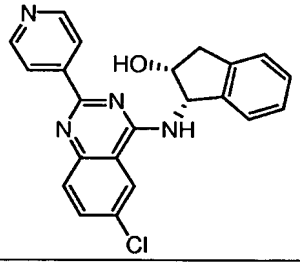
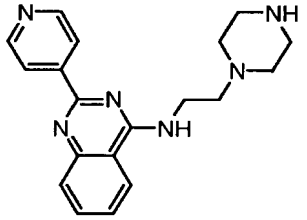
#	Name	Structure
27	(1R,2S)-1-[(2-phenylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
28	(1R,2R)-2-[(2-phenylquinazolin-4-yl)amino]cyclopentanol	
29	(1R,2R)-2-[(2-phenylquinazolin-4-yl)amino]cyclohexanol	
30	(1S,2R,3R,5R)-3-(hydroxymethyl)-5-[(2-phenylquinazolin-4-yl)amino]cyclopentane-1,2-diol	
31	(1S,2R)-1-[(6-chloro-2-pyridin-4-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
32	N-(2-piperazin-1-ylethyl)-2-pyridin-4-ylquinazolin-4-amine	

Table 3

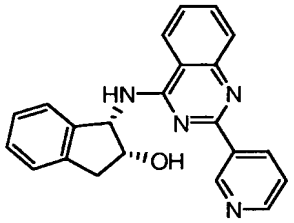
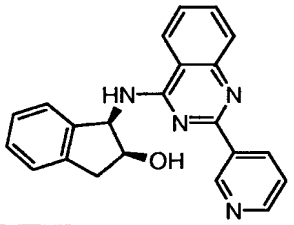
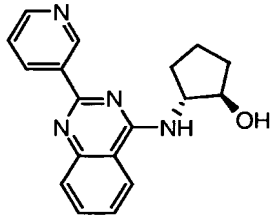
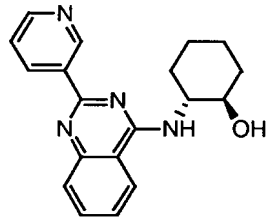
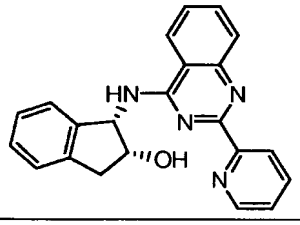
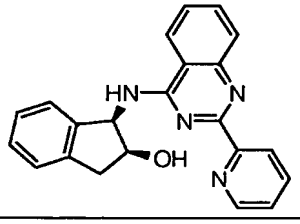
#	Name	Structure
33	(1S,2R)-1-[(2-pyridin-3-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
34	(1R,2S)-1-[(2-pyridin-3-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
35	(1R,2R)-2-[(2-pyridin-3-ylquinazolin-4-yl)amino]cyclopentanol	
36	(1R,2R)-2-[(2-pyridin-3-ylquinazolin-4-yl)amino]cyclohexanol	
37	(1S,2R)-1-[(2-pyridin-2-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
38	(1R,2S)-1-[(2-pyridin-2-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	

Table 3

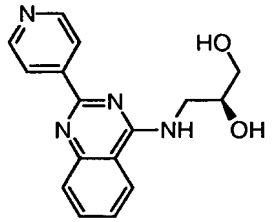
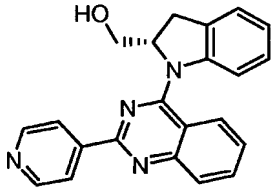
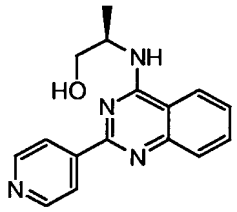
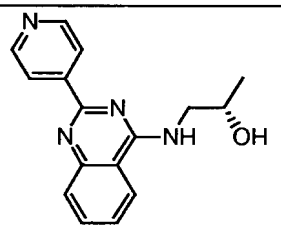
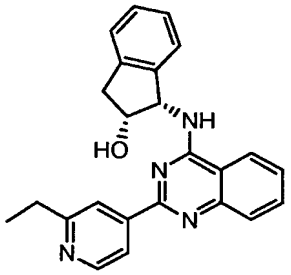
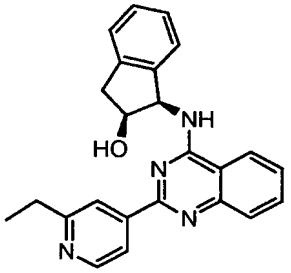
#	Name	Structure
39	(2S)-3-[(2-pyridin-4-ylquinazolin-4-yl)amino]propane-1,2-diol	
40	[(2S)-1-(2-pyridin-4-ylquinazolin-4-yl)-2,3-dihydro-1H-indol-2-yl]methanol	
41	(2R)-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-1-ol	
42	(2S)-1-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-2-ol	
43	(1S,2R)-1-{[2-(2-ethylpyridin-4-yl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	
44	(1R,2S)-1-{[2-(2-ethylpyridin-4-yl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	

Table 3

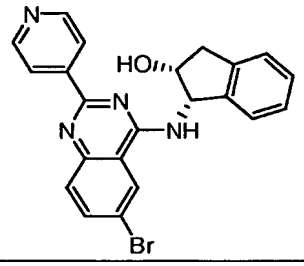
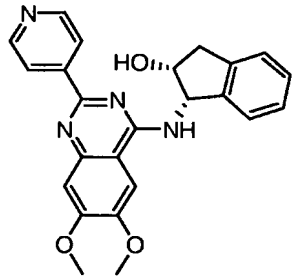
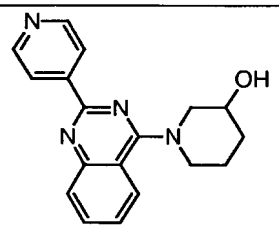
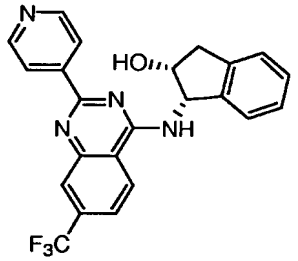
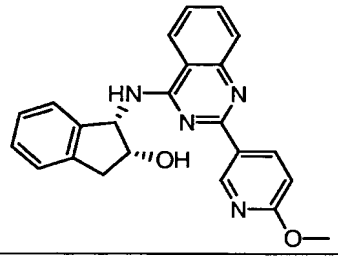
#	Name	Structure
45	(1S,2R)-1-[(6-bromo-2-pyridin-4-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
46	(1S,2R)-1-{[6,7-bis(methyloxy)-2-pyridin-4-ylquinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	
47	1-(2-pyridin-4-ylquinazolin-4-yl)piperidin-3-ol	
48	(1S,2R)-1-{[2-pyridin-4-yl-7-(trifluoromethyl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	
49	(1S,2R)-1-({2-[6-(methyloxy)pyridin-3-yl]quinazolin-4-yl}amino)-2,3-dihydro-1H-inden-2-ol	

Table 3

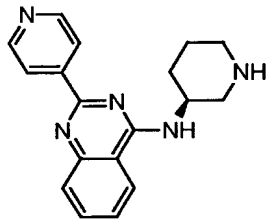
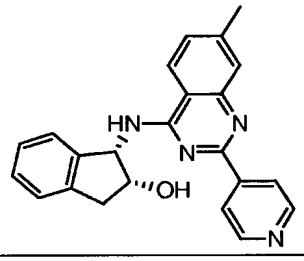
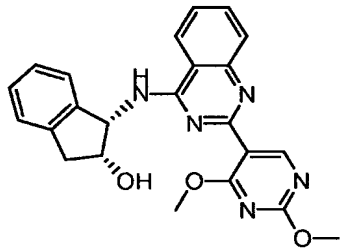
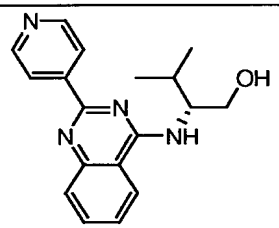
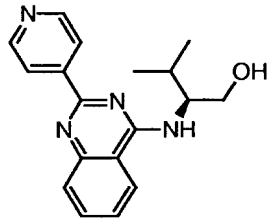
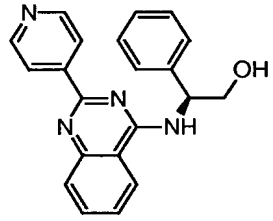
#	Name	Structure
50	N-[(3S)-piperidin-3-yl]-2-pyridin-4-ylquinazolin-4-amine	
51	(1S,2R)-1-[(7-methyl-2-pyridin-4-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
52	(1S,2R)-1-({2-[2,4-bis(methyloxy)pyrimidin-5-yl]quinazolin-4-yl}amino)-2,3-dihydro-1H-inden-2-ol	
53	(2R)-3-methyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]butan-1-ol	
54	(2S)-3-methyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]butan-1-ol	
55	(2S)-2-phenyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]ethanol	

Table 3

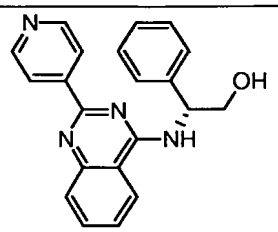
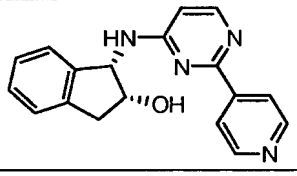
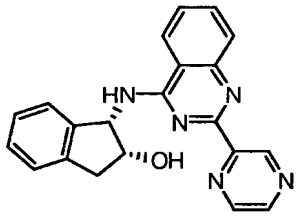
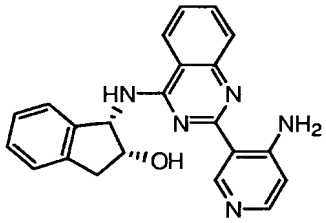
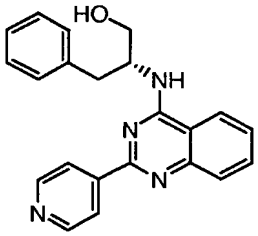
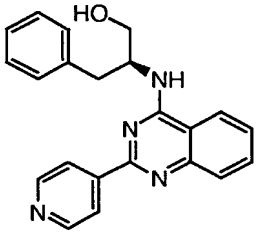
#	Name	Structure
56	(2R)-2-phenyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]ethanol	
57	(1S,2R)-1-[(2-pyridin-4-ylpyrimidin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
58	(1S,2R)-1-[(2-pyrazin-2-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
59	(1S,2R)-1-{[2-(4-aminopyridin-3-yl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	
60	(2R)-3-phenyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-1-ol	
61	(2S)-3-phenyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-1-ol	

Table 3

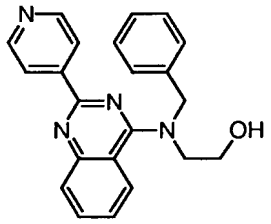
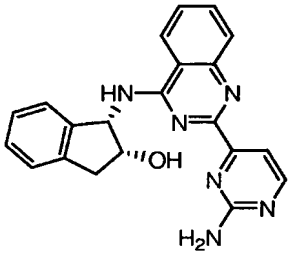
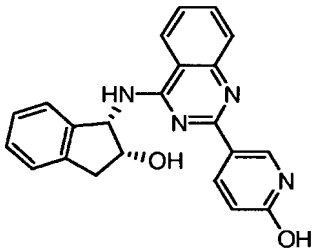
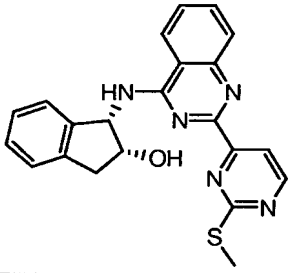
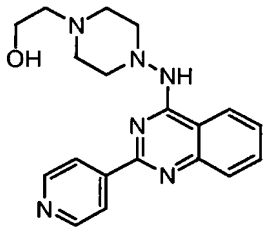
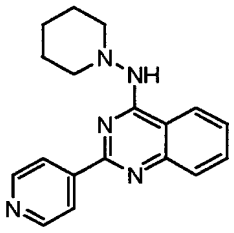
#	Name	Structure
62	2-[(phenylmethyl)(2-pyridin-4-ylquinazolin-4-yl)amino]ethanol	
63	(1S,2R)-1-{[2-(2-aminopyrimidin-4-yl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	
64	5-(4-{[(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}quinazolin-2-yl)pyridin-2-ol	
65	(1S,2R)-1-({2-[2-(methylthio)pyrimidin-4-yl]quinazolin-4-yl}amino)-2,3-dihydro-1H-inden-2-ol	
66	2-{4-[(2-pyridin-4-ylquinazolin-4-yl)amino]piperazin-1-yl}ethanol	

Table 3

#	Name	Structure
67	N-piperidin-1-yl-2-pyridin-4-ylquinazolin-4-amine	

19. A pharmaceutical composition comprising the compound according to any one of claims 1 - 18 and a pharmaceutically acceptable carrier.

20. A metabolite of the compound or the pharmaceutical composition according to any one of claims 1 -18.

21. Use of a compound according to any of claims 1 - 18 in the preparation of a medicament for modulating the *in vivo* activity of a kinase, for treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, or for inhibiting proliferative activity in a cell.

22. The use according to claim 21, wherein the kinase is Tie-2.

23. The use according to claim 22, wherein modulating the *in vivo* activity of Tie-2 comprises inhibition of Tie-2.

24. A method of screening for a modulator of a Tie-2 kinase, the method comprising combining either a composition comprising at least one of the compound according to any of claims 1 -18 and the pharmaceutical composition according to claim 31, and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.

Retyl421